Remarks/Arguments

Reconsideration of this Application and entry of this Amendment is respectfully requested. By the amendments, the Applicant does not acquiesce to the propriety of any of the Office's rejections and does not disclaim any subject matter to which the Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

The Applicant would like to thank the Office for its reconsideration and withdrawal of the 35 U.S.C. §112, first paragraph rejection of claim 13.

In the Claims

Claims 1, 5-6, 13-15, 19 and 21 are pending in this application. Claims 2-4, 7-12, 16-18, and 20 previously have been canceled. No new matter is added by way of this amendment. The Applicant reserves the right to pursue any excised or unclaimed subject matter in continuing applications.

Claims 1 and 13 have been amended to include the limitation "wherein said pressure sore is a result of immobility of a patient." Support for this amendment can be found in, for example, paragraph [0065] of the published specification.

Claim 14 has been cancelled as a result of its incorporation into claims 1 and 13.

35 U.S.C. §102 Rejections

I. Claims 1, 5-6, 15, 19, and 21 are rejected under 35 USC 102(e) as anticipated by U.S. Pat. Pub. 2005/0196414 (hereinafter "Dake"). The Applicant respectfully disagrees.

The Dake application was filed on March 3, 2005 and claims priority to provisional patent application No. 60/550,015 filed March 3, 2004.

Appended to this response is the 37 CFR §1.131 declaration of Stephen Donovan (hereinafter "Mr. Donovan") who is Vice Persistent and Assistant General Counsel for Allergan, Inc. The declaration states that Mr. Donovan has the authority to

sign the 37 CFR §1.131 declaration on behalf of Allergan, Inc. The inventor and assignor to Allergan, Inc. of the present application, Dr. Eric R. First is no longer an employee of Allergan, Inc., and Dr. Eric R. First is not available to sign the 37 CFR §1.131 declaration. The declaration further states that the claimed invention was conceived prior to March 3, 2004. Dake can only be asserted as a reference under 35 U.S.C. §102(e) as of its earliest effective U.S. filing date, which is March 3, 2004. The concurrently-filed declaration and the evidence submitted therewith establish that the claimed invention was conceived before March 3, 2004.

Therefore, the Applicant has established that Dake is not prior art to the present application, and therefore, cannot be used as the basis of the rejection under 35 U.S.C. §102(e). Accordingly, the Applicant respectfully requests withdrawal of this 35 U.S.C. §102(e) rejection.

II. Claim 1 also is rejected under 35 USC 102(b) as anticipated by *The New England Journal of Medicine*, Vol. 341, No. 2, pp. 65-69 (1999) (hereinafter "Brisinda"). The Office asserts that Brisinda teaches a method of treating anal fissures and that such an embodiment is within the scope of the claimed methods. The Applicant respectfully disagrees.

Section 2131 of the M.P.E.P. requires a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). As such, the reference used to reject a claim under 35 U.S.C. §102(b) must teach each and every limitation of the claim either expressly or inherently.

Claim 1 as presently amended includes the limitation "wherein said pressure sore is a result of immobility of a patient." The Applicant asserts that Brisinda teaches methods of treating anal fissures in which "[s]pasm of the anal sphincter has been noted in association with[.]" (page 65, column 2). Brisinda is teaching a method of treating an anal fissure resulting from muscle spasms with botulinum toxin or nitroglycerine. The presently amended claim 1 recites a method of treating a pressure sore resulting from

patient immobility (i.e., lying in bed, sitting in a wheel chair, and/or wearing a cast for a prolonged period of time (paragraph [0002] of published specification)), not from repeated spasms of the anal sphincter. Therefore, Brisinda does not teach, nor can be fairly interpreted to suggest, a method of teaching treatment of a pressure sore utilizing botulinum toxin, wherein said pressure sore is a result of immobility of a patient.

Further, claim 1 recites "wherein the therapeutically effective amount of a botulinum toxin type A is less than an amount that would be used to paralyze a muscle." Brisinda is teaching of a method of treating anal fissures by intramuscularly injecting botulinum toxin to paralyze the anal sphincter muscles, thereby reducing the contractions of/in the anal sphincter muscles. The presently amended claims recite a method of delivering a therapeutically effective amount of botulinum toxin which is less than an amount that would be used to paralyze a muscle. Therefore, Brisinda does not teach a method of delivering a therapeutic amount of botulinum toxin wherein the therapeutically effective amount of a botulinum toxin type A is less than an amount that would be used to paralyze a muscle.

As such, Brisinda does not teach each and every limitation of the presently amended claim 1 either expressly or inherently. Therefore, the Applicant requests the Office withdraw the 35 U.S.C. §102(b) rejection of claim 1.

III. Claim 13 is rejected under 35 USC 102(b) as being anticipated by Gregory c. Oliver, Md, FACS, ACS Spring Meeting 2002, slide 35 (hereinafter "Oliver"). The Office asserts that Oliver teaches a method of treating anal fissures comprising the steps of administering BOTOX® type A (30 units) and debriding a chronic fissure wound, specifically an anal fissure.

Section 2131 of the M.P.E.P. requires a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). As such, the reference used to reject a claim under 35 U.S.C. §102(b) must teach each and every limitation of the claim either expressly or inherently.

The Applicant asserts that the presently amended claim 13 recites that the pressure sore is a result of immobility of a patient. Oliver is teaching of a method of treating anal fissures by intramuscularly injecting botulinum toxin to paralyze the anal sphincter muscles (See slide 15 entitled "Injection of Internal Sphincter and Fissure"), thereby reducing the pressure in the anus contractures of the anal sphincter muscles. Oliver does not teach of a method of treating pressure sores resulting from patient immobility.

The presently amended claim 13 additionally recites a method wherein the therapeutically effective amount of a botulinum toxin type A is less than an amount that would be used to paralyze a muscle. Oliver teaches a method of injecting the anal sphincter with 30 units of botulinum toxin type A. Methods are known in the art of intrasphincter injection of, for example, "about 30-80 units of BOTOX® to treat constipation by intrasphincter injection of the puborectalis muscle" (paragraph [0036] of the published specification). Injections such as these are intramuscular injection with a therapeutic goal of at least partially paralyzing the sphincter. Therefore, Oliver does not teach a method of delivering a therapeutic amount of botulinum toxin wherein the therapeutically effective amount of a botulinum toxin type A is less than an amount that would be used to paralyze a muscle, because Oliver is delivering an amount of botulinum toxin type A that should at least partially paralyze the sphincter muscle.

As such, Oliver does not teach each and every limitation of the presently amended claim 13 either expressly or inherently. Therefore, the Applicant requests the Office withdraw the 35 U.S.C. §102(b) rejection of claim 13.

35 U.S.C. §103 Rejections

Claims 1, 5-6, 14-15, 19 are rejected under 35 USC §103(a) as being unpatentable over U.S. Pat. Pub. 2003/0021776 ("Rebar") in view of U.S. Pat. Pub. 2002/0187164 ("Borodic") and U.S. Pat. 6,447,787 ("Gassner"). The Applicant respectfully traverses.

The Office asserts that Rebar describes, suggests and teaches a method of treating a pressure sore (paragraph [310]) by subcutaneously administering (paragraph [0291]) a composition that comprises a *Clostridium perfringens* iota toxin together with a zinc finger protein (ZFP), the toxin being used to translocate the ZFP across a cell membrane. The Office suggests that the teachings of Rebar differ from the claimed invention in that they failed to show that the toxin was a *Clostridium botulinum* toxin, specifically type A. The Office provides Borodic who teaches *Clostridium perfringens* iota toxin and *Clostridium botulinum* toxin C2 to be functional equivalents (paragraph [0028]). The Office further provides Gassner which the Office suggests teaches *Clostridium botulinum* toxin C2 and type A (col. 3, lines 43-46) both function as chemodenervating agents for the purpose of enhancing wound healing through minimizing the adverse effects of muscle tension and movement on the wound during healing.

The Applicants respectfully appreciate the Office's arguments regarding the present 35 U.S.C. §103(a) rejection, however, the Applicant disagrees with the Office's analysis of the references and the conclusions drawn therefrom and asserts that the Office has failed to establish a *prima facie* case of obviousness.

Obviousness is a question of law based on underlying factual inquiries. MPEP § 2141(II). Support for any 35 U.S.C. § 103 rejection must include a "clear articulation of the reason(s) why the claimed invention would have been obvious." MPEP § 2142, citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007). The Office bears the initial burden of factually supporting a *prima facie* conclusion of obviousness, and if the examiner does not meet this burden, the Appellant is "under no obligation to submit evidence of nonobviousness." MPEP § 2142.

Further, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All the words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Rebar is directed to zinc finger protein's (ZFP) ability to treat ischemia and facilitate wound healing (see abstract). Rebar tangentially discloses that "[t]oxin molecules also have the ability to transport polypeptides across cell membranes" (paragraph [0275]). Despite the fact that that Rebar generically discloses "toxin molecules" as carriers, the Office opines that a skilled artisan in view of Rebar would be inspired to instead use toxin molecules as an active agent. Then, the Office opines, a skilled artisan further would modify this circuitous interpretation of Rebar by substituting botulinum toxin type A for *Clostridium perfringens* iota toxin.

However, case law dictates that "[i]f a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Rebar teaches the use of ZFPs to treat ischemia and facilitate wound healing either alone or in combination with a carrier. In one embodiment, Rebar suggests the carrier may be a toxin. In order to modify the teachings of Rebar to arrive at the teachings suggested by the Office, wherein a toxin is delivered alone, a skilled artisan would end up with an embodiment that would be unsatisfactory for the intended purposes of Rebar. A ZFP is required to treat ischemia and facilitate wound healing according to the teachings of Rebar. When combined with Borodic and Gassner, the resulting teachings would not motivate a skilled artisan to modify Rebar according to the Office's assertions. Therefore, Rebar has not been properly applied by the Office.

Further, although Rebar tangentially discloses *Clostridium perfringens* iota (paragraph [0275]), it is an entirely different species from botulinum toxin type A. As the present specification discloses, the "genus *Clostridium* has more than one hundred and twenty seven species" with botulinum being but one of those species. Further, botulinum toxin serotype A is one of seven immunologically distinct botulinum toxin serotypes (published specification [0017]). Therefore, it would not have been obvious to one skilled in the art to merely replace one toxin for another.

Case law has additionally established that "[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents." *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958).

The Office has attempted to combine Borodic with the teachings of Rebar suggesting that Borodic teaches *Clostridium perfingens* iota toxin and *Clostridium botulinum* C2 toxin are functional equivalents. However, Borodic states "Clostridium botulinum C2 toxin, Clostridium perfingens iota toxin, and Clostridium spiroforme toxin act on ADP-ribosylate actin monomers." (paragraph [0028]). The Applicant asserts that Borodic is not teaching the equivalency of *Clostridium perfingens* iota toxin and *Clostridium botulinum* C2 toxin, but rather pointing out that the two toxins may function through acting on the same actin monomers. As such, the Office has improperly relied on *Clostridium perfingens* iota toxin and *Clostridium botulinum* C2 toxin as mere functional equivalents.

Borodic does not motivate the skilled artisan to substitute a botulinum toxin for *Clostridium perfringens* iota toxin and a skilled artisan would not view these entirely different species of toxin as substitutable. Contrary to the Offices assertion, Borodic does not teach that *Clostridium botulinum* C2 toxin serves to translocate the ZFP across a cell membrane. Furthermore, there is no teaching in Borodic as to how a different species of *Clostridium* toxin would work as a carrier for ZFPs. Further, Borodic does not teach or reasonable suggest wound healing. Rather, Borodic applies "botulinum toxin to a number of patients with a variety of neuralgia-related facial pains . . . ." (paragraph [0028]). A skilled artisan would not combine Borodic's teaching of a facial pain treatment with botulinum toxin type A to modify Rebar's teaching of the combined administration of ZFPs and *Clostridium perfringens* iota as a carrier for the ZFPs.

Gassner does nothing to remedy the shortcomings of Rebar and Borodic. The claims as presently amended recite "wherein said pressure sore is a result of immobility of a patient" and locally administering a therapeutically effective amount of a botulinum toxin…wherein said therapeutically effective amount is less that an amount of botulinum

toxin that would be used to paralyze a muscle." However, Gassner's wounds are those that are "adversely affected by muscle tension or movement" (col. 3, lines 6-8). As such Gassner does not teach a method of treating a pressure sore resulting from the immobility of a patient, as is presently claimed. Rather, Gassner teaches of a method of treating wounds affected by muscle tension or movement and thereby reducing the appearance of scars (see abstract). Gassner states, "[p]aralysis of the underlying muscle activity increases the rate of healing and yields a better cosmetic result. Without being bound by a particular mechanism, locally induced paralysis of the musculature subjacent to a cutaneous defect is thought to minimize the repetitive tensile forces on the wound edges, resulting in superior cosmetic outcome in the resultant scar." (column 2, lines 56-62). As such, Gassner teaches a method of paralyzing muscles in an effort to decrease muscle tension and movement, thereby aiding in healing and a reduction in scaring. That is contrary to the presently amended claims which recite "less that an amount of botulinum toxin that would be used to paralyze a muscle." Further, the methods of the present claims are drawn to pressure sores that result from a lack of movement of a patent, not as a result of excess tension or movement as is taught by Gassner. As such, the combination of Rebar, Borodic and Gassner do not teach each and every limitation of the presently amended claims either expressly or inherently.

Further, there would be no motivation to modify Gassner, even when combined with Rebar and Borodic because paralysis of musculature is key to Gassner's teachings. In order to modify the teachings of Gassner to arrive at the teachings suggested by the Office, wherein a toxin is delivered to treat skin wounds without paralyzing the musculature, a skilled artisan would end up with an embodiment that would be unsatisfactory for the intended purposes of Gassner. In other words, if a skilled artisan was to modify the teachings of Gassner thereby not paralyzing the musculature, the teachings of Gassner would not be functional for its intended purpose, because a muscle paralysis is required to enhance wound healing according to the teachings of Gassner.

As such, Rebar can not be used for its intended purpose when modified to be combined with Borodic and Gassner, as such, the reference has not been used properly

by the Office. Additionally, Gassner can not be used for its intended purpose when modified to be combined with Rebar and Borodic. Even IF Rebar was successfully combined with Borodic and Gassner or IF Gassner was successfully combined with Rebar and Borodic, all claim limitations are not taught by a combination of the cited references, and therefore, no *prima facie* case of obviousness has been established by the Office and the Applicant requests the Office withdraw the 35 U.S.C. §103(a) rejection of claims 1, 5-6, 14-15 and 19.

Conclusion

Applicant respectfully requests that a timely Notice of Allowance be issued in this case. The Commissioner is authorized to charge any fee which may be required in connection with this Amendment, or credit any overpayment, to deposit account No. 50-3207.

Respectfully submitted,

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